I CLAIM:

1. A method of identifying a ligand capable of binding to at least one determinant of a biologically active site on a target, which determinant participates in conferring biological activity of said target, the method comprising:

a) providing at least one reporter antibody to be used as a reporter of binding of said ligand to the biologically active site, and wherein said antibody is selected from an antibody library of sufficient diversity to possess at least one antibody member capable of binding to at least one determinant in the biologically active site as determined by the ability of said antibody member, either alone or in combination with at least one other ligand, to possess agonist or antagonist activity;

b) identifying as potential ligands for activity at the target, those ligands which are capable of competing with the reporter antibody for binding to the target.

2. The method according to claim 1 wherein the reporter antibodies are members of a recombinant library wherein each antibody member (rVab) of the recombinant library comprises at least one variable region selected from the group consisting of VH and VL regions, and optionally comprising a constant domain attached by its amino terminus to the variable region.

3. The method according to claim 2 wherein the rVab unit is displayed on the surface of a carrier.

4. The method according to claim 2 wherein the rVab unit is soluble.

5. The method according to claim 3 wherein the carrier is a bacteria.

6. The method according to claim 3 wherein the carrier is a bacteriophage.

7. The method according to claim 2 wherein a parental VL region comprising at least one CDR is used to derive the VL region of the rVab by deleting, inserting or substituting at least one amino acid within at least one CDR.

8. The method according to claim 2 wherein a parental VH region comprising at least one CDR is used to derive the VH region of the rVab by deleting, inserting or substituting at least one amino acid within at least one CDR.

9. The method according to claim 2 wherein parental VL and VH regions comprising at least one CDR, are used to derive a pair of VL and VH regions of a rVab by deleting, inserting or substituting at least one amino acid within at least one CDR of each variable region.

10. The method according to any one of claims 7, 8 or 9 wherein the crystal structure of the parental V regions used to derive rVab are known.

11. The method according to claim 9 wherein the crystal structure of the parental VH and VL pair used to derive the rVab is known.

12. The method according to claim 2 wherein at least one of the parental V regions used to derive rVab is unmodified.

13. The method according to claim 2 wherein the crystal structure of the rVab is determined after isolation as

a rVab which binds to a biologically active site on the target.

14. The method according to claim 2 wherein at least two V regions are modified by deleting, inserting or substituting at least one amino acid in at least one CDR after isolation as rVab which binds to a biologically active site on the target.

15. The method according to claim 1 wherein the target is a polypeptide, protein, nucleic acid, oligosaccharide, carbohydrate or lipid.

16. The method according to claim 1 wherein activity of the target is coupled to an assayable biochemical response at the target which biochemical response functions as a signal of target activation.

17. The method according to claim 16 wherein the biochemical response is detectable as a change in a protein or polypeptide characteristic.

18. The method according to claim 16 wherein the biochemical response is associated with an organometallic moiety, a metal or other nonprotein.

19. The method according to claim 16 wherein the biochemical response is associated with a portion of the bioactive structure.

20. The method according to claim 16 wherein the biochemical response comprises a detectable free radical, fluorescent or chemiluminsecent group, radioactive isotope or involves oligomerization.

21. The method according to claim 16 wherein the biochemical response is phosphorylation and the signal is a change in the phosphorylation state of the target.

22. The method according to claim 17 wherein the signal protein is a G protein and the signal is a change in either the prepense of a G protein regulatory agent or the binding of rVab due to the presence of a G protein regulatory agent.

23. The method according to claim 16 wherein the signal is a change in the binding of rVab to its binding site.

24. The method according to claim 2 wherein the recombinant antibody comprises a single polypeptide chain comprising a VH functionally coupled to a VL to produce a binding site.

25. A method of identifying ligands capable of binding to at least two determinants which together are required for biological activity of a pharmacological target, the method comprising:

a) screening and isolating from an rVab library, rVab members comprising at least one VH and VL regions, and optionally comprising a constant domain attached by its amino terminus to the V region, and capable of binding to at least one of the determinants of the pharmacological target;

b) making and expressing an rVab-peptide (rVab-PEP) library comprising the isolated rVab members coupled to at least one peptide comprised of a random sequence of amino acids;

c) screening the rVab-PEP library for first rVab-Pep members which bind and activate the pharmacological

target wherein the rVab component binds to a first determinant of the pharmacological target and the peptide component binds to a second determinant of the pharmacological target;

d) screening the rVab-Pep library and identifying a second rVab-pep member capable of actively binding to the pharmacological target, and wherein the rVab component binds to a third determinant of the pharmacological target and the peptide component binds to fourth determinant of the pharmacological target.

26. The method according to claim 25 wherein the rVab component of the second rVab-Pep member competes with the peptide component of the first rVab-Pep member for binding to a determinant on the pharmacological target.

27. The method according to claim 25 wherein the rVab component of the first rVab-Pep member competes with the peptide component of the second rVab-Pep member for binding to a determinant on the pharmacological target.

28. The method according to claim 25 wherein the first determinant of the pharmacological target is the same as the fourth determinant, and wherein the second determinant of the pharmacological target is the same as the third determinant.

29. The method according to claim 25 wherein the rVab component used to construct the rVab-Pep has at least one other attribute of an active ligand, besides affinity for the target, and wherein the attribute is selected from selectivity and biological activity.

30. The method according to claim 29 wherein rVabs which bind to determinants of active sites are identified by

their ability to competitively or allosterically alter the binding on an endogenous ligand.

31. The method according to claim 25 wherein the active rVab-Pep possess agonist or antagonist activity.

32. The method according to claim 31 wherein activity of the target is coupled to an assayable biochemical response at the target which biochemical response functions as a signal of target activation.

33. The method according to claim 32 wherein the biochemical response is detectable as a change in a protein or polypeptide characteristic.

34. The method according to claim 32 wherein the biochemical response is associated with an organometallic moiety, a metal or other nonprotein.

35. The method according to claim 32 wherein the biochemical response is associated with a portion of the bioactive structure.

36. The method according to claim 32 wherein the biochemical response comprises a detectable free radical, fluorescent or chemiluminsecent group, radioactive isotope or involves oligomerization.

37. The method according to claim 32 wherein the biochemical response is phosphorylation and the signal is a change in the phosphorylation state of the target.

38. The method according to claim 33 wherein the signal protein is a G protein and the signal is a change in

either the prepense of a G protein regulatory agent or the binding of rVab due to the presence of a G protein regulatory agent.

39. The method according to claim 32 wherein the signal is a change in the binding of rVab to its binding site.

40. The method according to claims 25 wherein the peptide component of the rVab-Pep members comprising VH and CL regions are expressed attached to either or both of the amino terminus of VH and the carboxy terminus of CL.

41. The method according claim 40 wherein the peptide component is attached to the amino terminus of the VH region.

42. The method according to claim 40 wherein the peptide component is attached to the carboxy terminus of the CL region.

43. The method according to claim 40 wherein two peptides are attached to the rVab component to form rVab-Pep^2.

44. The method according to claim 40 wherein the peptide comprises between about 5 and 50 amino acids.

45. The method according to claim 44 wherein the peptide comprises between about 7 and 25 amino acids.

46. The method according to claim 45 wherein the peptide comprises about 8 amino acids.

47. A reporter of binding of a ligand to a determinant of a pharmacological target, which target requires binding of ligand to at least two determinants of said target to produce a biological response, said reporter comprising an rVab portion of an active rVab-Pep, and wherein said rVab component of said rVab-Pep binds to a first determinant of said target, and the peptide component binds to a second determinant of said target.

48. The reporter of claim 47 wherein the rVab comprises VH and CL regions and the peptide is expressed bound to either or both of the amino terminus of the VH and the carboxy terminus of the CL.

49. The reporter according claim 48 wherein the peptide component is attached to the amino terminus of the VH region.

50. The reporter according to claim 47 wherein the peptide component is attached to the carboxy terminus of the CL region.

51. The method according to claim 47 wherein two peptides are attached to the rVab component to form rVab-Pep^2.

52. The method according to claim 47 wherein the peptide comprises between about 5 and 50 amino acids.

53. The method according to claim 52 wherein the peptide comprises between about 7 and 25 amino acids.

54. The method according to claim 53 wherein the peptide comprises about 8 amino acids.

55. A method of identifying a ligand capable of binding to at least one determinant of a biologically active site on a target, which target requires activation of at least two determinants to express biological activity of said target, the method comprising:

a) providing at least one rVab reporter antibody according to claim 47 to be used as a reporter of binding of said ligand to the biologically active site, and wherein said antibody is selected from an antibody library of one antibody member capable of binding to at least one determinant in the biologically active site as determined by the ability of said antibody member, either alone or in combination with at least one other ligand, to possess agonist or antagonist activity;

b) identifying as potential ligands for activity at the target, those ligands which are capable of competing with the reporter antibody for binding to the target.

56. The method according to claim 55 wherein multiple ligands are identified which when bound together covalently, are capable of binding to the determinants necessary to cause a bioligical response of the target, the method comprising:

a) providing reporter rVab antibodies for each of the determinants for which ligands are to be identified;

b) for each of the rVab reporter antibodies, identifying as potential ligands for activity at each of the determinants of the target, those ligands which are capable of competing with each of the rVab reporter antibodies for binding to the target;

c) covalently linking the identified ligands so as to form active multivalent ligands capable of activating the pharmacological target.

57. The method according to claim 56 wherein the identified ligands are non-protein organic molecules.

58. The method according to claim 56 wherein the two rVab reporter antibodies are used to identify two ligands which are combined to form the multivalent active ligand.

59. The method according to claim 56 wherein the pharmacological target is a polypeptide receptor.

60. A recombinant rVab antibody library comprising rVab members possessing at least one VL or VH region derived from a parental variable region with at least one CDR which is diversified to form different rVab members by deleting, inserting or substituting at least one amino acid within at least one CDR.

61. The recombinant antibody library according to claim 60 wherein a parental VH region comprising at least one CDR is used to derive the VH region of the rVab members by deleting, inserting or substituting at least one amino acid within at least one CDR.

62. The recombinant antibody library according to claim 60 wherein parental VL and VH regions comprising at least one CDR, are used to derive a pair of VL and VH regions of rVab members by deleting, inserting or substituting at least one amino acid within at least one CDR of each variable region.

63. The recombinant antibody library according to any one of claims 60, 61, or 62 wherein the crystal structure of the parental V regions used to derive rVab members are known.

64. The recombinant antibody library according to claim 60 wherein the crystal structure of the parental VH and VL pair used to derive the rVab members is known.

65. The recombinant antibody library according to claim 60 wherein at least one of the parental V regions used to derive rVab is unmodified.

66. The recombinant antibody library according to claim 60 wherein the CDR regions of a specific antibody are expressed on a plurality of frameworks which provides for variable geometric orientation of the CDR regions.

67. The recombinant antibody library according to claim 60 wherein the rVab members further comprise a peptide sequence covalently bound to the rVab members to form rVab-Pep members.

68. The recombinant antibody library according to claim 67 wherein the peptide component of the rVab-Pep members comprising VH and CL regions are expressed attached to either or both of the amino terminus of VH and the carboxy terminus of CL.

69. The recombinant antibody library according claim 68 wherein the peptide component is attached to the amino terminus of the VH region.

70. The recombinant antibody library according to claim 68 wherein the peptide component is attached to the carboxy terminus of the CL region.

71. The recombinant antibody library according to claim 68 wherein two peptides are attached to the rVab component to form rVab-Pep^2.

72. The recombinant antibody library according to claim 68 wherein the peptide comprises between about 5 and 50 amino acids.

73. The recombinant antibody library according to claim 72 wherein the peptide comprises between about 7 and 25 amino acids.

74. The recombinant antibody library according to claim 73 wherein the peptide comprises about 8 amino acids.

75. A method of providing a model for a ligand capable of binding to a determinant of an active site of a pharmacological target, the method comprising:

a) providing at least two rVab identified as binding to an active surface of a pharmacological target;

b) identifying the regions of the rVabs that bind the biologically active site or individual inactive surface determinants of the bioactive structure;

c) grouping the rVabs by overlapping structures which bind to common epitopes;

d) determining the relative spatial orientation, charge and energetics of the identified binding sites

e) determining the molecular structure necessary to bind the target and confer activity.